Remarks

Claims 1, 3-12, and 29-56 are pending.

Claims 1, 5, and 52 have been amended to recite that the claimed vaccine "does not cause unfavorable reactions." Support for this amendment is found in the specification, at page 23, lines 2-3: "No unfavorable reactions resulting from the vaccine's use have been reported;" page 23, lines 14-15: "No unfavorable reactions in animals receiving the product have been reported;" page 20, line 1: "No injection reactions were observed;" and the abstract: "These vaccines demonstrate no undesirable side effects ..."

The Applicants thank the Examiner for indicating that the objections and rejections under 35 U.S.C. §112 have been withdrawn.

The rejections under 35 U.S.C. §102(b)

The rejection based on Boothby, Immunologic Responses to Mycoplasma bovis, University Microfilm International (Dissertation) 1-172, 1982 (Boothby I)

Claims 1, 3, 5, 6, 29, 30, 40-44, and 52-55 have been rejected as being anticipated by Boothby I.

Claims 1, 3, 5, 6, and 52-55

Independent claims 1, 5, and 52 have been amended to recite that the claimed vaccine "does not cause unfavorable reactions." Dependent claims 3, 6, and 53-55 therefore also now carry this recitation. Accordingly, all of claims 1, 3, 5, 6, and 52-55 carry this limitation.

There is a clear difference between the Applicants' vaccine and Boothby I's vaccine. Boothby I's vaccine produces a very unfavorable reaction - all of Boothby I's animals showed hypersensitivity (see Boothby I, page 136, 3rd paragraph: "All groups receiving adjuvant preparations developed delayed-type hypersensitivity ..."). This is a real functional difference between the Applicants' vaccine and Boothby I that must be due to the nature of the vaccine, and cannot be attributed to any "intended use" of the vaccine.

In addition to the above considerations, claims 5, 6, 52, 54, and 55 are not anticipated by Boothby I for the following reasons.

Claim 5 and dependent claims 6 and 54 require that the vaccine comprises particular biotypes that are not disclosed in Boothby I. Thus, Boothby I cannot anticipate these claims. Claim 52 recites that the vaccine comprises an adjuvant that differs from the adjuvants listed in Boothby I.[1] Therefore, Boothby I does not anticipate claim 52. Claim 55 depends from claim 52 and therefore Boothby I does not anticipate claim 55 either.

In view of the above, it is respectfully requested that this rejection be withdrawn with respect to claims 1, 3, 5, 6, and 52-55.

Claims 29, 30, and 40-44

Claims 29, 30, and 40-44 all contain the limitation that the claimed vaccine must be "protective against *Mycoplasma bovis* mastitis in a bovine species." The Office Action states that this limitation is merely an "intended use" and therefore is not

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[1] At page 131, Boothby I discloses the use of the following adjuvants:
Freund's incomplete adjuvant
N-acetylmuramyl-L-alanyl-D-isoglutamine (MDP)
Amphotericin B
Combined magnesium/aluminum hydroxide
Killed *Bordatella pertussis*

sufficient to avoid anticipation by Boothby I. See the Office Action, sentence bridging pages 4 and 5: "If the prior art is capable of performing the intended use, then it meets the claim."

The Applicants do not agree. Being protective against mastitis is not simply an intended use but rather is a functional characteristic of the vaccine itself. Case law holds that vaccines can be patentable over prior art based on such functional characteristics. See Ex parte Plotkin, 174 USPQ 39 (Pat. Off. Bd. App. 1971). In Plotkin, the claimed vaccine had the functional characteristic of being able to be administered intranasally with high effectiveness. This was found to confer patentability to claims to the vaccine itself over the prior art.

The characteristic of being protective against mastitis distinguishes the claims over the prior art, such as the vaccine disclosed in Boothby I. Given that the vaccine in Boothby I clearly differs from the Applicants' vaccine (as shown by differences with respect to causing unfavorable reactions), it cannot be assumed that Boothby I's vaccine is protective against mastitis. Thus, there has been no *prima facie* showing of anticipation.

Furthermore, even if a *prima facie* showing of anticipation had been made, the evidence of record is sufficient to rebut such a showing since the evidence of record demonstrates that Boothby I's vaccine was not protective against mastitis. For example, Heller et al., 1993, Vet. Microbiol. 37:127-133[2] did not mention that one should vaccinate to control mastitis but instead stated that culling is necessary. See page 127: "To control the spread of this disease, an early detection of the pathogen is crucial since the removal and culling of infected cows is necessary to prevent fresh infections." In Hanson, (September, 2001) Bovine Veterinarian 4-8[3] and Hanson, (October, 2001) Bovine Veterinarian 12-20[4], methods to prevent mastitis or mitigate its effects are

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[2] Reference A32 of the Information Disclosure Statement filed April 16, 2002.

[3] Reference A30 of the Information Disclosure Statement filed April 16, 2002.

[4] Reference A31 of the Information Disclosure Statement filed April 16, 2002.

described but the methods do not include vaccination, indicating that no effective vaccine was known to the art.

The Office Action dismissed this evidence by stating: "Applicants referral to other publications (Heller et al, 1993, Hanson, September 2001 and Hanson, October 2001) to support their position is irrelevant since Boothby teach the claimed vaccine compositions." [emphasis added] However, this misunderstands the import of the evidence. Heller and the two Hanson publications demonstrate that Boothby I does not teach the claimed vaccines. The Applicants submit that the Office Action has assumed the issue to be decided – whether Boothby I discloses the claimed vaccines –before considering all the evidence that should be used to decide that issue. The U.S. Patent & Trademark Office has the burden of proving a case of anticipation, based upon reasoned arguments, after considering all relevant evidence. The Applicants submit that this has not been done.

The Office Action did not explain why, if Boothby I provided a vaccine against mastitis, the art was still recommending culling and other non-vaccine approaches as the only methods of combating mastitis long after Boothby I's disclosure became public. Based on the record as it currently stands, the inevitable conclusion is that Boothby I's vaccine was not protective against mastitis, and thus could not have been the same as the claimed vaccine.

In re Casey, 152 USPQ 235 (CCPA 1967) is not applicable to the present application because the functional properties of the claimed device in Casey were found to be inherently disclosed in the Kienzle prior art reference. See 152 USPQ at 238, where the Court of Customs and Patent Appeals agreed with the reasoning of the Board of Appeals and stated: "The rationale of the board clearly deducible from the language employed is that the Kienzle apparatus as it obviously must be constructed would inherently perform all of the functions called for in claim 1 ..." In the present application, the functional property of being protective against mastitis is not found in the prior art.

In In re Otto, 136 USPQ 458 (CCPA 1963), the claims were rejected for obviousness over a large number of references that collectively disclosed all the limitations recited in the claims. That is not the case here, where the record contains no prior art disclosing the limitation of "protective against bovine mastitis." Instead, the record contains compelling evidence that the prior art lacked this limitation.

A decision which dealt with functional characteristics of product claims and is applicable to the present application is Union Oil Co. of Cal. v. Atlantic Richfield Co., 54 USPQ2d 1227 (Fed. Cir. 2000). In Union Oil, the claims at issue were directed to gasolines that were defined as being suitable for combustion in automotive engines. See 54 USPQ2d at 1231:

> The claims of the '393 patent recite either "[a]n unleaded gasoline suitable for combustion in an automotive engine" or "[a]n unleaded gasoline fuel suitable for combustion in a spark ignition automotive engine."

The district court construed these claims to cover only automotive fuels, not also aviation or racing fuels. This was primarily due to the specification's teaching that the functional characteristic of being suitable for use in automotive engines addressed the problem the invention was directed toward, together with the claims' recitation of that characteristic. This resulted in a finding that the quoted functional language was a real limitation of the claims, and not just an intended use. See 54 USPQ2d at 1231-1232:

> The district court's interpretation also finds extensive support in the specification. The patentees described the problem that their invention addressed:
>
> > One of the major environmental problems confronting the United States and other countries is atmospheric pollution (i.e., "smog") caused by the emission of gaseous pollutants in the exhaust gases from automobiles. This problem is especially acute in major metropolitan areas, such as Los Angeles, Calif., where the atmospheric conditions and the great number of automobiles account for aggravated air pollution.
>
> ...
>
> The patentees tailored their research and their patent to ordinary fuels for use in standard passenger cars. Thus, the claim language, further informed by the specification, shows that the district court correctly read the claims to cover ordinary automotive fuel.
>
> Because the '393 patent covers only standard automotive fuel, the district court correctly determined that specialty fuels within other limitations of the claims do not anticipate under 35 U.S.C. § 102.

As in Union Oil, claims 29, 30, and 40-44 of the present application recite the functional characteristic at issue – "protective against *Mycoplasma bovis* mastitis." Also as in Union Oil, the present specification stresses the problem of mastitis and teaches that the vaccines of the present invention address that problem by providing actual data that show the vaccines to be protective against mastitis. See page 2, lines 1-11:

> Diseases caused by mycoplasmas are often resistant to antimicrobial therapy, leaving no effective means of treatment. Consequently, the only effective control method is to cull animals from a herd. This has enormous economic implications in the dairy industry where losses are measured by the value of the culled animals as well as the impact on both milk quality and quantity due to clinical and subclinical infections. Mycoplasma infections resulting in bovine mastitis are increasing in prevalence and geographical distribution. In the United States, this higher prevalence is due to a larger and-more intense cattle production industry in which herds are rapidly expanding, placing them at greater risk. Increased incidence of *M. bovis* infection and related infectious disease in dairy herds has been noted worldwide (Jasper, DE 1982, J. Amer. Vet. Med. Assn. 181:158-162).

See also Example 5, pages 18-20, where a large decrease in number of mastitis cases occurred in a herd that was vaccinated with the vaccine of the present invention. See in particular page 19, lines 17-32:

> Comparative results were used to measure efficacy of the vaccine. Samples taken from all animals presenting with clinical mastitis were cultured by an independent laboratory to monitor the absence or presence of Mycoplasma bovis infection of the mammary gland. Field evaluations were made by comparing clinical incidence of mastitis caused by Mycoplasma bovis following herd vaccination to the base line herd incidence prior to vaccination. Results were as follows:
>
> Pre Vaccination Base Line Incidence:
> 155 confirmed positive clinical Mycoplasma bovis infections
>
> Post Vaccination Herd Incidence:
> 1st year following vaccination:
> 24 confirmed positive clinical Mycoplasma bovis infections
> 2nd year following vaccination:
> 1 confirmed positive clinical Mycoplasma bovis infection.

In view of the Federal Circuit's guidance in Union Oil as to how such a claim recitation should be construed, the recitation of "protective against *Mycoplasma bovis* mastitis" is a true limitation of claim 29, 30, and 40-44 and serves to distinguish these claims over the prior art.

Even if the recitation of "protective against bovine mastitis" is viewed as an intended use, this rejection should be withdrawn. In connection with the interpretation

of this recitation as an intended use, the Office Action cited Casey and Otto as support for the proposition that (sentence bridging pages 4 and 5) "If the prior art is capable of performing the intended use, then it meets the claim."

Where the prior art product was not capable of performing the intended use, the Board of Patent Appeals and Interference held that claims were not anticipated. In Ex parte Hervy A. Morris (available at 1998 WL 1736155, copy enclosed), a claim directed to a cutting device recited "to deflect the liquid jet stream when the cutting element is moved to the idle position." The Examiner interpreted this recitation as an intended use and rejected the claim over Casey and Otto, stating: "If the prior art structure is capable of performing the intended use, then it meets the claim."

> [t]he phrase "to deflect the liquid-jet stream ....." should not be construed as defining structure. It does not describe any structure; it merely expresses what the disk is desired to do. However, it has well been established that, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In re Casey, [370 F.2d 576, 580,] 152 USPQ 235[[, 238] (CCPA 1967); In re Otto, [312 F.2d 937, 940,] 136 USPQ 458, 459 (CCPA 1963).

Ex parte Hervy A. Morris, page 2.

The Board of Patent Appeals and Interference reversed this rejection, stating:

> Although we appreciate the examiner's position, we do not agree with his argument, because in our view the disk 620 of Driver is not capable of performing the intended use recited, i.e., of "deflect[ing] the liquid-jet stream when the cutting element is moved to the idle position."

Ex parte Hervy A. Morris, page 2.

The evidence of record shows that Boothby I's compositions were not "capable of performing the intended use" because the evidence of record shows that Boothby I's compositions were not protective against mastitis. Accordingly, Casey and Otto are not applicable and claims 29, 30, and 40-44 are not anticipated by Boothby I.

In view of the above, it is respectfully requested that this rejection be withdrawn with respect to claims 29, 30, and 40-44.

The rejection based on Thorns et al., 1980, Res. Vet. Sci. 29:328-332 (Thorns)

Claims 1, 4, 5, 7, 29, 30, and 56 have been rejected as being anticipated by Thorns.

Claims 1, 4, 5, 7

Thorns does not anticipate claims 1, 4, 5, and 7 because Thorns does not disclose at least the following three limitations of claims 1, 4, 5, and 7:

- "does not cause unfavorable reactions"
- "vaccine"
- "an adjuvant"

Does not cause unfavorable reactions

Independent claims 1 and 5 have been amended to recite that the claimed vaccine "does not cause unfavorable reactions." Dependent claims 4 and 7 therefore also now carry this recitation.

There is a clear difference between the vaccines of claims 1, 4, 5, and 7 and Thorn's mycoplasma strains. The vaccines of claims 1, 4, 5, and 7 do not cause unfavorable reactions while the strains of Thorns cause unfavorable reactions. All of the strains in Thorns caused some kind of histopathological change. See the right column in Table 1 on page 329, which shows that only the control (i.e., no *Mycoplasma bovis*) injections resulted in no histopathological changes.

Vaccines

Furthermore, claims 1, 4, 5, and 7 are directed to "vaccines" that are protective against diseases caused by *Mycoplasma bovis* in bovines. Thorns does not disclose a vaccine. Thorns discloses attenuated strains of *Mycoplasma bovis* that were injected into mice. There is no disclosure in Thorns that the attenuated strains were protective against any disease in the injected mice. Thorns does not even disclose any data that indicate the attenuated strains caused any stimulation of the immune systems of the mice against *Mycoplasma bovis*.

Thorns showed that highly passaged strains were attenuated in the sense that they did not cause responses such as inflammation or abnormal glands to the same degree as low passaged strains. Thus, Thorns disclosed attenuated *Mycoplasma bovis* strains. But claims 1, 4, 5, and 7 are not directed simply to attenuated strains. They are directed to attenuated strains that are capable of functioning as vaccines. Thorns contains no evidence that the attenuated strains disclosed therein could function as vaccines, to protect against disease caused by later exposure to *Mycoplasma bovis*. In particular, Thorns provided no evidence that the mice that were given the attenuated strains were protected from disease when later challenged with *Mycoplasma bovis*. Apparently, Thorns did not even challenge the mice.

Moreover, the authors of Thorns did not consider that their strains were vaccines. The authors considered that the work they disclosed provided information and a starting point for research that might someday "perhaps" lead to the production of a vaccine against *Mycoplasma bovis*. See page 332, right column, 3rd paragraph:

> Whatever mechanisms the virulent strains have lost or modified, they should provide further insight into the pathogenesis of *M. bovis* mastitis which could perhaps lead to a stable vaccine for this disease. [emphasis added]

The last phrase of this sentence makes clear that the authors of Thorns did not think that they have already provided such a vaccine.

Since claims 1, 4, 5, and 7 are directed to vaccines, and Thorns did not disclose vaccines, Thorns does not anticipate claims 1, 4, 5, and 7.

An adjuvant

Furthermore, claims 1, 4, 5, and 7 recite "an adjuvant." Thorns does not disclose an adjuvant. For this reason as well, Thorns does not anticipate claims 1, 4, 5, and 7.

Claims 29, 30, and 56

Claim 29, 30, and 56, like claims 1, 4, 5, and 7 discussed above, are directed to "vaccines." Since Thorns does not disclose vaccines, Thorns does not anticipate claims 29, 30, and 56.

Furthermore, claims 29, 30, and 56 recite the limitations that the claimed vaccines must be "protective against *Mycoplasma bovis* mastitis" (claims 29 and 30) or "protective against *Mycoplasma bovis* clinical disease ... wherein the clinical disease includes respiratory pneumonia" (claim 56). As discussed above in connection with the rejection over Boothby I, these recitations are functional limitations that confer patentable distinction on the claims. Thorns contains no showing that the attenuated strains disclosed therein are capable of protecting against any diseases. Thus, for this reason as well, Thorns does not anticipate claims 29, 30, and 56.

In view of the above, it is respectfully requested that this rejection over Thorns be withdrawn.

The rejections under 35 U.S.C. §103(a)

Claims 1, 3-12, and 29-56 have been rejected as being obvious over Boothby I in view of Poumarat et al., 1994, Vet. Microbiol. 40:305-321 (Poumarat) and Thorns.

Claims 1, 3-7, and 52-55

Claims 1, 3-7, and 52-55 recite that the vaccine "does not cause unfavorable reactions." As discussed above, this limitation is lacking in Boothby I and Thorns,

since the *M. bovis* in Boothby I caused hypersensitivity and the *M. bovis* in Thorns caused histopathological changes. Thus, these two publications lack a disclosure of this claim limitation.

As explained more fully below, Poumarat did not disclose vaccines of any kind, and thus did not teach or suggest a vaccine that does not cause unfavorable reactions.

In view of the complete lack of disclosure of this limitation in the prior art, the Applicants submit that a *prima facie* case of obviousness for claims 1, 3-7, and 52-55 has not been made. Accordingly, it is respectfully requested that this rejection of claims 1, 3-7, and 52-55 be withdrawn.

Claims 8-12, 31-39, and 46-51

Claims 8-12, 31-39, and 46-51 recite "at least two" *M. bovis* biotypes.

Boothby I does not disclose a vaccine that contains more than one biotype. Even if Thorns is viewed as disclosing vaccines (which the Applicants dispute), Thorns still does not disclose a vaccine containing more than one biotype since all the strains in Thorns were administered individually.

Poumarat does not disclose any vaccines since Poumarat is limited to a study of the antigenic characteristics of certain strains of *Mycoplasma bovis*. Moreover, Poumarat teaches away from the use of more than one biotype.

Poumarat divided *Mycoplasma bovis* isolates into 13 different "genomic groups." Poumarat then looked at the antigenic variability between and among these genomic groups. Although Poumarat found much antigenic variability, this variability did not correlate with membership in any particular genomic group. In other words, the same amount of antigenic variability could be found within groups as between groups. See page 318, 2nd paragraph:

> Antigenic profiles of the *M. bovis* strains obtained by immunoblotting with J008 calf serum differed markedly one from the other, the heterogeneity being equally great among

> strains belonging to the same genomic group and those coming from different genomic groups. There appeared to be no relation between the genomic variability of *M. bovis* and the antigenic variability ...

Because Poumarat teaches that antigenic variability is as great within *Mycoplasma bovis* groups as across *Mycoplasma bovis* groups, Poumarat teaches that there would be no gain in antigenic variability from including more than one type of *Mycoplasma bovis* in a vaccine. That is, there would be no point in having more than one type of *Mycoplasma bovis* in a vaccine. Poumarat thus discourages one of ordinary skill in the art from including more than one biotype in a vaccine.

Poumarat's teaching away is especially pertinent in connection with claims 34-39 and 46-51. These claims all require that the at least two biotypes be genetically different, as judged by analysis of DNA or RNA. Poumarat teaches that such genetic differences are irrelevant with respect to antigenicity since Poumarat teaches that there appears to be "no relation between the genomic variability of *M. bovis* and the antigenic variability." One of ordinary skill in the art would interpret this as a teaching that nothing is to be gained from including biotypes that are genetically different in a vaccine and thus would be led away from the invention of claims 34-39 and 46-51.

In view of the above, it is respectfully requested that this rejection of claims 8-12, 31-39, and 46-51 be withdrawn.

Claims 29, 30, and 40-45

Claims 29, 30, and 40-45 recite that the vaccine is "protective against *Mycoplasma bovis* mastitis."

None of Boothby I, Thorns, or Poumarat disclose or suggest this limitation.

Furthermore, there was a long-felt need in the art for an effective vaccine against bovine mastitis. See, e.g., Hanson, (September, 2001) Bovine Veterinarian 4-8 (Hanson I) and Hanson, (October, 2001) Bovine Veterinarian 12-20 (Hanson II), which contain

extensive descriptions of the problems caused by bovine mastitis and the difficulty of dealing with this disease. For example, Hanson I quotes a veterinarian as follows (page 4):

> "*Mycoplasma* mastitis is a doubly insulting disease," says Blackmer. "Not only can it be remarkably contagious when it is present but it absolutely does not respond to antibiotic therapy. In fact, treatment can actually cause epidemics, because it frequently is spread by unsound intramammary therapy practices."

The art also discloses that others tried and failed to produce a vaccine protective against mastitis. Boothby et al., 1986, Can. J. Vet. Res. 50:200-204 (Boothby II)[5] shows this failure of others, and also teaches away from the present claims. Boothby II tested whether killed *M. bovis* would be effective as a vaccine against bovine mastitis and found that it was not. Despite their prior exposure to killed *M. bovis*, the treated cows in Boothby II were not protected against infection (see page 202, middle column: "All experimentally challenged quarters became infected ..."). Thus, Boothby II was unsuccessful. Certainly it must be admitted that failure is a deterrent. The skilled person therefore would have been deterred by Boothby II from attempting to produce *M. bovis* vaccine and thus from seeking the solution provided by the Applicant.

Moreover, the treated animals in Boothby II showed poorer milk production than the untreated animals. The treated cows suffered significant and persistent reductions in the level of milk production. The control cows exhibited a smaller and more transient drop in milk production. See Figure 2 on page 202 for a comparison of treated and control cows. Thus, not only did the killed *M. bovis* fail to protect the treated cows, but it caused milk production to be even worse than it would have been had the cows not been treated. Since an important purpose for having dairy herds is to produce milk, one of ordinary skill in the art would certainly be deterred by a result that decreased the production of milk.[6] Given that Boothby would have deterred the skilled person in two

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[5] Reference A17 of the Information Disclosure Statement filed April 16, 2002.

[6] This is recognized by Boothby II at page 200, right column, where it is stated: "If prophylactic vaccination is to be efficacious, it must have minimal effects on the health and productive capabilities of the cow."

major respects – lack of efficacy and decrease in milk production – Boothby must be seen as teaching away from the Applicant's invention.

In view of the above, it is respectfully requested that this rejection of claims 29, 30, and 40-45 be withdrawn.

Claim 56

Claim 56 is directed to attenuated vaccines that are protective against respiratory pneumonia.

Boothby I and Poumarat do not disclose attenuated *Mycoplasma bovis*. As discussed above, Thorns does disclose attenuated strains of *Mycoplasma bovis* but states that these strains are not vaccines, but might provide "further insight" which could "perhaps" lead to the development of a vaccine. See Thorns, page 332, right column, 3rd paragraph:

> Whatever mechanisms the virulent strains have lost or modified, they should provide further insight into the pathogenesis of *M. bovis* mastitis which could perhaps lead to a stable vaccine for this disease. [emphasis added]

Given the lack of disclosure of an attenuated vaccine that is protective against respiratory pneumonia in Boothby I, Thorns, and Poumarat, and the lack of any suggestion as to how such a vaccine could be produced in those references, it cannot be said that those references make obvious claim 56.

In view of the above, it is respectfully requested that this rejection of claim 56 be withdrawn.

The time for responding to the Office Action was set for August 25, 2005. Enclosed herewith is a Petition for the Extension of Time under 37 C.F.R. § 1.136(a) for a period sufficient to permit the filing of this response. Please charge any corresponding fees for the Petition to Kenyon & Kenyon's Deposit Account No. 11-0600.

The Applicants hereby make a Conditional Petition for any relief available to correct any defect seen in connection with this filing, or any defect seen to be remaining in this application after this filing. The Commissioner is authorized to charge Kenyon & Kenyon's Deposit Account No. 11-0600 for the Petition fee and any other fees required to effect this Conditional Petition.

Respectfully submitted,

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